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Hydrogels Based on Polyvinylpyrrolidone Copolymers

Oleh Suberlyak and Volodymyr Skorokhoda

Additional information is available at the end of the chapter

Abstract

The role of polyvinylpyrrolidone (PVP) complex formation with water-soluble 2-hydroxy-alkyl methacrylates is described. The impact of the complexation on both the polymerization kinetics and the formation of a copolymer structure initiated by radical initiators has been studied. The activating effect of iron(II) and iron(III) sulfates has been revealed for the initiator-free polymerization of the formulation. An analytical approach to determining the molecular weight of the chain fragments located between two neighboring cross-linking nodes in the polymer network (Mn) has been developed depending on the values of the stability constant (Kst) for the charge-transfer complexes. The basic regularities of hydrogels obtaining based on PVP copolymers with high sorption capacity and diffusion characteristics are presented. The main directions of practical application of synthesized hydrogels are considered.

Keywords: hydrogels, polyvinylpyrrolidone, complex with charge transfer, cross-linked copolymers, permeability membranes, capsulation particles, drugs, soft contact lenses, biomedical, properties

1. Introduction

The concentration of colloid polymer solutions is accompanied by increasing viscosity up to a critical value when a gel is formed. A gel (a jellylike material) is a system which exhibits no flow and is based on a fluctuation polymer network swollen in a solvent. The formation of gels is accompanied by the appearance of physical nodes between macromolecular chains. The stability of fluctuation nodes and, therefore, the gel stability increase with increasing energy of the interaction between solvent molecules and polymer chains. In the case of using aqueous solutions of natural or synthetic polymers, a "hydrogel" is formed. This is a hydrogel of the "second type." Such a product consists of two phases and is unstable. During significant change of temperature or dynamic load it divides into two phases that hydrogel—formed a

syneresis process occurs [1]. That is why a gel of the "second type" cannot be recommended for long-lasting exploitation under variable conditions.

Polymeric gels of the "first type" are formed upon swelling of chemically cross-linked hydrogels, and their matrix consists of macromolecule segments located between chemical cross-linking nodes. It leads to the formation of chemically cross-linked network that swells due to the sorption of a solvent. Chemical bonds between macromolecules provide non-fluidity of the system. Network swells partially as a result of change of the segment conformation under the effect of a solvent.

Conformational static macromolecular coil (**Figure 1**) of chain segments between cross-linking nodes causes significant reversible deformation which corresponds to highly elastic deformation under the influence of external force field. Hydrogels are formed during the swelling of chemically cross-linked highly hydrophilic polymers in water. A large number of hydrogels, obtained through the polymerization in water or in bulk with the following swelling of the synthesized polymer in water, are known [2].

Water-soluble monomers such as vinylpyrrolidone [3], hydroxyalkyl (met)acrylates (HAMA) [4–6] and their homologs (C_3–C_{13}) [7], propylene glycol methacrylates [8], etc. are used for the synthesis of a polymer matrix.

In the method [9], a chemically cross-linked structure is formed due to the usage of a bifunctional monomer of similar nature in reaction mass. Cross-linking agents (CA), which are used for the polymerization of monofunctional monomers, are bis-(met)acrylates of glycols [10–14], bis-allylic esters [15, 16], triallyl cyanurate [17], dialdehydes [18], and polyethylene glycol dimethacrylates [19].

The number of CA affects the degree of polymer matrix cross-linking and molecular weight of intermolecular crosslinks [20].

Content of water can vary from 5 to 90% depending on the quantity of cross-linking agent and its molecular weight [20, 21]. The quantity of CA with low molecular weight, such as dimethacrylates, can be 0.25–2%, which would provide a sufficient amount of water in a hydrogel [22–24]. It has been mentioned that hydrogels based on hydroxyalkyl (met)acrylates, used for production of contact lenses, have quite low oxygen permeability. Oxygen permeability of hydrogel with 28% of water is $35 \cdot 10^{-10}$ cm$^2 \cdot$mL O$_2$/mL$\cdot$s$\cdot$mm.
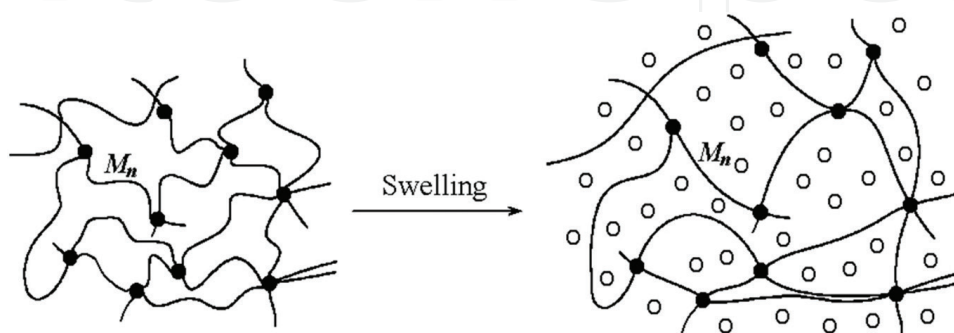

Figure 1. Schematic diagram of swelling of hydrogel [(●) cross-linking node and (○) water molecule].

It has been stated [25] that oxygen permeability depends just on the water content and does not depend on the chemical structure of a hydrogel matrix.

A highly hydrophilic matrix of a hydrogel can also be obtained due to chemical cross-linking of water-soluble polymers. For example, polyvinyl alcohol (PVA) cross-linked by heating in the presence of sodium tetraborate [26] or by initiated graft polymerization, in particular, PVA with glycidyl methacrylate [27]. To this end, polyvinylpyridine, poly(ethylene glycol), and hydroxypropyl cellulose are also applied besides PVA. [13, 15, 28–31]. Such polymers are mainly used for the reduction of internal tensions due to them washing out during hydration process and increase of matrix-free volume that decreases spatial obstacles for the conformational changes of structured polymer chains.

Method of grafted copolymerization of water-soluble monomers on polyvinylpyrrolidone (PVP) appears to be particularly promising with significant possibilities of hydrogel polymeric matrix formation [32, 33]. PVP is used by itself as a sorbent, a thickener of cosmetic ointments and for encapsulation of medical drugs [34]. Due to its high surface energy, PVP is also an attractive (a promising) substance in the formation of metal nanopowders [35, 36] as well as silicate nanopowders from corresponding solutions [37]. PVP keeps adsorbed drugs on the pyrrolidone rings of the macromolecule [38, 39].

Macromolecule of PVP in a free state has a helicoidal structure with pyrrolidone rings outside, which promotes the interaction of the peptide groups with substances by complex formation. PVP is characterized by high complexation ability. It forms complexes with organic and inorganic electron donor as well as electron acceptor compounds. Complexes form highly polarized peptide groups of the pyrrolidone rings due to mesomeric effect. Specific role is played by complexes of PVP with vinyl monomers which polymerize in the presence of PVP.

2. Role of polyvinylpyrrolidone in the kinetics and formation of structure

Important and notable property of PVP is the ability to form complexes [40–42]. This ability significantly influences the kinetic of polymerization and the formation of a polymeric matrix structure in the process of hydrogel synthesis.

As it has been shown in the research papers [43, 44], PVP can form charge-transfer complexes not only with medical drugs but also with water-soluble vinyl monomers. The results of spectral analysis and quantum mechanical calculations with the application of package Chem3D [45] shows that $-C = C-$ bond of a monomer molecule, negative charge of which significantly changes, and nitrogen atom of the pyrrolidone cycle $(-N-)$, the charge of which increases from +0.35 to +0.42, both participate in the formation of a complex (**Figure 2**).

The complex was characterized by the constant of complex stability (K_{st}), and its value increases with the presence of water or primary alcohol groups [43, 46]. Based on this information, the structure of a charge-transfer complex (CTC) with, for example, 2-hydroxyethyl methacrylate (HEMA) was substantiated [33, 46].
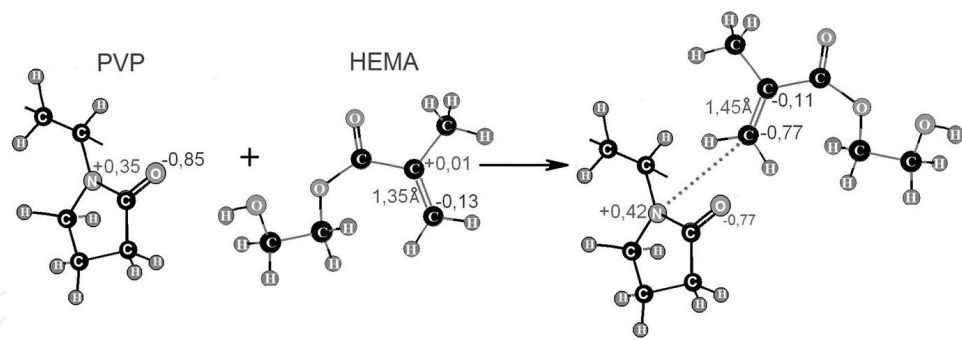
Figure 2. Quantum mechanical model of interaction by PVP with HEMA.

The constant of stability of CTC represents fraction of quantity of the molecules of a reaction mixture (molecules of monomer and elementary links of PVP), which form CTC, to their general quantity in the volume. The change of optical density of diluted solutions of the monomer and PVP in a chosen solvent is determined.

As a result of the monomer molecule solvation on the PVP macrochains through CTC, the rate of HEMA [43] polymerization increases significantly. The rate constant of the polymerization significantly depends on K_{st} of CTC. The polymerization rate increases with the increase of K_{st} of CTC with the maximum at the equimolar ratio of a proton donor (H_2O) and segments of PVP (**Table 1**) [47].

An activation effect of PVP can be observed in proton donor solvents and allows the polymerization without initiators of radical type [48].

The results prove the matrix mechanism of polymerization—local concentration of monomer molecules activated with CTC on the chains of PVP.

Solvent	K_{st} (dm³/mole)	Extinction coefficient (dm³/(mole·cm))	Viscosity[1], (η·10³, Pa·sec)	$V^1 \cdot 10^4$ (mole/ (dm³·sec) (at 60°C))	Degree of PVP graft, P, %
Dimethyl sulfoxide	0	–	2.4	0	–
Cyclohexanol	0.06	20.8	17.6	0.6	11
Butanol	0.12	10.0	2.1	0.8	–
Ethylene glycol	0.17	5.6	14.4	1.1	14
Diethylene glycol	0.21	2.1	22.3	1.5	15
Water	0.28	5.3	5.3	3.8	18

[1] Comment: HEMA-PVP: solvent = 9:1:10 mass parts (without initiator), initiator-benzoperoxide.

Table 1. Influence of the nature of solvents on the stability constant of the complex and on the polymerization rate (V) of HEMA-PVP composition.

Such mechanism allows to explain the formation of grafted and few structured PVP copolymer [62]:

1. Adsorption of an initiator and solvation of a monomer on PVP macromolecules and formation of change transfer complex

2. Initiation

3. Chain growth

4. The chain transfer to the PVP as from initial radical $R^\bullet$ and from macroradical $R_m^\bullet$

5. Graft copolymerization on PVP

Obtaining of grafted copolymers as a result of macroradical combination.

The degree of grafting of PVP depends on the nature of a complex-forming solvent and the nature of an initiator of polymerization of HEMA-PVP compositions (**Table 1**).

Matrix effect increases with the increase of hydroxyl group number in the solution and with the increase of the molecular weight of a proton donor. As a result, CTC with polyvinyl alcohol as a proton donor was found to have significant activating ability [49].

This method allowed to obtain hydrogels with higher mechanical resistance based on the combined matrix PVP:PVA [49, 50]. Complex based on the PVA and PVP shows the highest efficiency at the ratio of 2:1 (**Table 2**).

Efficiency of grafting (f) (inclusion of PVP macromolecules into the copolymer structure or its chemical cross-linking), and also cross-linking degree of macrochains in a polymer network (M_n), first of all depends on the value of stability constant of CTC (**Figure 3**) [47]. During polymerization of HEMA:PVP composition, K_{st} was changed by the replacement of certain amount of water for the acceptor of protons (dimethyl sulfoxide (DMSO)).

Composition of forming solution (mass parts)				M_n (kg/mole)	Tensile strength (σ, MPa)	Relative elongation at rupture (ε, %)
PVP	PVA	HEMA	H_2O			
–	30	30	200	15	10.5	500
25	5	30	200	175	0.29	281
25	10	30	200	180	0.45	390
30	15	15	200	185	0.21	260
25	10	30	200 DMSO	195	0.49	295
25	10	15 + 15 GMA	100 + 100 DMSO	146	0.87	510

Comments: M_n, molecular weight mass of the fragment of macrochain between two neighboring cross-linking nodes; GMA, glycidyl methacrylate.

Table 2. Physico-mechanical properties of membranes based on the hydrogels in hydrated state.
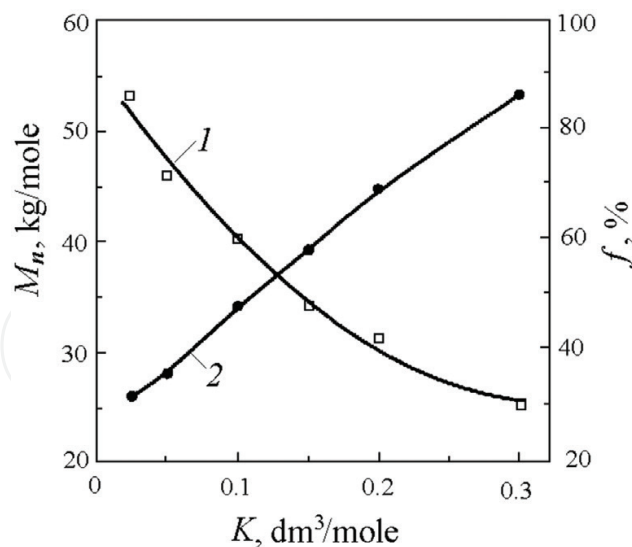
Figure 3. Dependences of the internodal molecular mass M_n (1) and grafting efficiency f (2) on the constant K of complex formation between 2-hydroxyethyl methacrylate and polyvinylpyrrolidone.

The molecular weight of the fragment of macrochain between two neighboring cross-linking nodes has been calculated according to the following formula:

$$M_n = \frac{L^5 \rho_p v_s}{0.5 - \mu} \tag{1}$$

where L is the linear swelling coefficient, ρ_p is the polymer density (kg/m^3), v_s is the molar volume of the solvent (m^3/(kg·mole)), and μ is the parameter of polymer-liquid interaction:

$$\mu = 0.5 - \frac{v_s \sigma_\infty L^4}{RT(\lambda^2 - \lambda^{-1})} \tag{2}$$

where σ_∞ is the equilibrium voltage (kgf/m^2):

$$\lambda = 1 + \varepsilon, \, 0 < \varepsilon < 0.3 \tag{3}$$

where ε is the equilibrium voltage strain.

Profitability for practical realization under the circumstances of predicted synthesis dependence of the M_n on the amount of DMSO as proton acceptor to water (A)

$$A = \ln \frac{6.25}{K_{st}} - 6.875 \tag{4}$$

Using this dependence, the exponential dependence of M_n on K_{st} is offered:

$$M_n = M_n^0 \cdot \exp(-2.9 \, K_{st}) \tag{5}$$

where M_n^0 is the molecular weight mass of the fragment of macrochain between two neighboring cross-linking nodes by $K_{st} = 0$ (in DMSO).

Contents of the components, mass parts				M_n (kg/mole)	K_{lt} (%)	σ (MPa)	ε (%)	$k \cdot 10^4$ (m³/(m²·h))
HAMA[1]	PVP	H₂O	DMSO					
80	20	100	0	24	95	0.40	235	52
80	20	99	1	25	95	0.40	235	53
80	20	90	10	31	95	0.41	240	57
80	20	80	20	41	95	0.41	245	63
80	20	70	30	52	95	0.42	250	70
80	20	60	40	65	95	0.42	255	76
80	20	40	60	67	—	—	—	77
80	20	80	20	38	96	0.43	230	57
80	20	80	20	44	94	0.40	240	70

Comments: In examples 1–7, we used 2-hydroxyethyl methacrylate as HAMA; in example 8, we used 2-hydroxypropyl methacrylate; and in example 9, we used 2-hydroxypropyl acrylate. DMSO, dimethyl sulfoxide; K_{lt} is the luminous transmission factor, and k is the permeability coefficient of water.

Table 3. Influence of the amount and nature of solvents on the properties of hydrogels.

The dependencies which are appropriate for analytical forecast of the copolymer structure have been proposed. The experimental results of synthesis of hydrogels based on HEMA/PVP at the various amounts of DMSO in the initial composition have been obtained (**Table 3**).

3. Effect of the amount of grafted PVP on the sorption parameters of copolymers

Hydrogels based on the structured hydrophilic copolymers can be obtained due to water sorption. Water sorption by this (co)polymers occurs up to equilibrium-limited swelling of polymeric matrix due to the presence of hydrophilic groups –OH, –C = O, –NH–, and –NH₂ in their structure. This process is going with different rates depending on the hydrophilic properties of polymer network and volume (bulk) of block sample.

Equilibrium swelling is characterized by the coefficient of swelling:

$$\text{Volume} \qquad \text{Mass} \qquad \text{Linear}$$
$$K_V = \frac{V_K}{V_0} \quad K_M = \frac{m_{max}}{m_0} \quad K_L = \frac{L_{max}}{L_0} \qquad (6)$$

The coefficient of linear swelling is within 1.13…1.20 [51], and the amount of water content is within 20…90%, which can be calculated with the equation:

$$W_{H_2O} = \frac{m_{max} - m_0}{m_{max}} \cdot 100\% \qquad (7)$$

where m_{max} is the mass of the sample after swelling and m_0 is the initial mass of the sample before swelling.

Hydrogel is also characterized by water sorption—the amount of water that can be sorbed by dry sample during swelling up to reaching the equilibrium state:

$$W_v = \frac{m_{EQ} - m_0}{m_0} \cdot 100\,\% .$$

(8)

In general, it is assumed that hydrogels based on the structured hydroxyalkyl (meth)acrylates contain 20–40% of water. It has been stated [52] that the amount of sorbed water for such hydrogels depends on the degree of polymeric matrix cross-linking or on the molecular weight of the polymeric grid fragment between nodes.

Hydrogels based on the synthetic copolymers of polyvinylpyrrolidone can be obtained by three methods:

By the method of free-radical thermopolymerization of water-soluble hydroxyalkyl (meth) acrylates in aqueous solution using water-soluble or alcohol-soluble peroxide initiators, at the temperature of 50–70°C. In this case, network structural parameters and water amount in the hydrogel depend on the amount of water in the reaction mass (**Table 4**) [20, 52]

Based on the reactivity of HEMA:PVP composition, a stable hydrogel can be formed in the process of polymerization in water solution when the amount of aqueous is two to three times higher than the mass of composition that forms polymeric matrix. Resulting hydrogel does not release excess of water due to its high sorption ability of PVP-based polymeric matrix and significantly smaller ratio of macrochain crosslinks (**Table 5**). However, under the major excess of water, resulting hydrogel has lower mechanical resistance (**Table 1**).

By the polymerization of PVP-monomer mixture at the room temperature under the effect of iron(II) sulfate in aqueous media, resulting in hydrogel formation (**Table 6**) [52].

Contents of the components for the preparation of membranes (mass parts)				Water content (%)	$k \cdot 10^4$ (m^3/ ($m^2 \cdot h$))	Permeability coefficient (mole/($m^2 \cdot h$))		
HEMA	PVP	H_2O	DMSO			Sodium chloride	Carbamide	Sucrose
100	—	100	—	40	5	80	13	5
80	20	100	—	48	52	181	36	14
80	20	95	5	48	55	193	—	—
80	20	90	10	47	57	212	—	—
80	20	80	20	47	63	240	—	—
80	20	200	—	55	74	234	59	30
80	20	300	—	61	90	263	60	31
70	30	100	—	53	71	232	59	30
50	50	100	—	61	102	274	65	33

Comments: For membranes 1–5, 8, and 9, the luminous transmission factor is 90–96%; membranes 6 and 7 are opaque.

Table 4. Sorption-diffusion properties of hydrogel membranes (δ = 0.2 mm).

Contents of the components (mass parts)				σ (MPa)	ε (%)
HEMA	PVP	H_2O	DMSO		
100	–	100	–	0.53	165
90	10	100	–	0.46	190
80	20	100	–	0.40	235
80	20	200	–	0.38	245
80	20	300	–	0.37	255
70	30	100	–	0.31	270
50	50	100	–	0.22	295
80	20	90	10	0.41	240
80	20	80	20	0.41	245

Comments: DMSO, dimethyl sulfoxide; σ, the ultimate strength of the film; ε, elongation at break of the film.

Table 5. Dependence of mechanical properties of hydrogels on composition content.

By polymerization in bulk of PVP-monomer mixture under the effect of peroxide or iron(II) sulfate initiators followed by swelling of obtained block in water (**Table 7**).

The degree of equilibrium swelling depends on the sorption ability of a copolymeric matrix. Sorption ability of copolymers, which contain in their structure macromolecules of PVP, is much higher than copolymers, based on the separate monomers dissolved in water (**Table 8**) [53].

Water, sorbed in the volume of hydrogel that is based on the monomer system, is in the two forms—filling free intermolecular volume (free water) and solubilized by polar groups in the form of H-complexes and solvated membranes [8, 53]. Water, associated with H-complexes on the polar groups of matrix, transfers into quasicrystal structure, decreasing mobility of water molecules. The higher amount of polar groups is in the polymeric grid; the higher is the water sorption ability of polymer (**Table 9**) [8, 20].

Blend composition (mass parts)		H	P	E	W	k
HEMA	PVP	(MPa)	(%)	(%)	(%)	
90	10	0.101	11	89	48	1.19
80	20	0.099	13	87	52	1.28
70	30	0.082	15	85	63	1.34
60	40	0.079	18	82	69	1.35
50	50	0.050	21	79	76	1.36

Comments: H, hardness number; E, elasticity index; P, plasticity index; W, water content; k, hydrogel swelling factor.

Table 6. Dependence of physical-mechanical properties of copolymers obtained in solution on the blend composition (T = 298 K, [FeSO$_4$] = 0.01%; blend:H$_2$O = 1:1).

[FeSO$_4$] (wt %)	M$_C$ (kg/mol)	ν (mol/kg)	f (%)	p (%)	Copolymer composition (wt %)	
					polyHEMA	PVP
0.01	15.8	0.063	76/91	15/19	84/82	16/18
0.03	14.8	0.067	77/67	15/14	84/86	16/14
0.05	13.6	0.074	79/59	16/13	83/87	17/13
0.07	13.2	0.076	82/37	17/8	83/92	17/8

Comments: numerator, values of block copolymers; denominator, values of copolymers synthesized in water (H$_2$O:blend = 1:1 w/w); M$_c$, molecular weight of the chain fragment between polymeric network points; ν, network density; f, grafting efficiency; p, grafting degree.

Table 7. Effect of FeSO$_4$ concentration on the grafting efficiency, grafting degree, and copolymer composition (T = 298 K; HEMA:PVP = 80:20 w/w) [52].

Contents of the components (mass parts)			M$_n$ (kg/mole)	Water content (W, %)	k·10^4 (m^3/(m^2·h))
HEMA	PVP	H$_2$O			
100	–	100	12	42	5.1
100 (T3EGDMA)	–	100 (ethanol)	–	1	0.8
80 (GMA)	20	100 (ethanol)	–	20	–
90	10	100	20	45	29.0
80	20	100	24	48	52.3
80	20	200	28	55	74.2
80	20	300	–	61	90.3
70	30	100	38	53	71.4
50	50	100	51	61	102.1
Methylcellulose membrane			–	–	4.0

Comments: k, the permeability coefficient of water; GMA, glycidyl methacrylate; T3EGDMA, triethylene glycol dimethacrylate.

Table 8. Dependence of M$_n$ and W$_{H2O}$ of hydrogels on composition contents.

For PVP sorption of water has specific characteristics.

(a) Hydrate membranes are formed as a result of physical interaction of water with PVP around its elements. In those membranes, due to hydrogen bonds between molecules of water and groups of –N-C = O, redistribution of electronic density occurs that might promote formation of hydroxonium on pyrrolidone cycles. Rothschild [54] offered the scheme of such interaction.

During this interaction of PVP with molecules of water series of changes in pyrrolidone ring occurs.

Content of the components for the preparation of membranes (mass parts)				Water content (W, %)	Coefficient of permeability	
					by water $K \cdot 10^4$ (m³/(m²·h))	by NaCl α (mole/(m²·h))
PVA	PVP	HEMA	H_2O			
30	–	30	200	84	52	404
5	25	30	200	75	150	320
10	25	30	200	80	280	320
15	30	15	200	81	280	437
–	–	100	100	40	5	80

Table 9. Sorption-diffusion parameters of hydrogel membranes (thickness 30 μm).

According to the authors [55, 56], about 70% of hydrolyzed rings form hydrogen bonds with water (H-complexes). At the same time, it was found that around such a ring 55 molecules of water are placed in the form of solvated layers—hydrate membranes. The polarization degree of water molecules depends on the distance from ligand-polarized group. Membranes are the least polarized at the external hydrate layers.

(b) Molecules of water that are located on the large distance from carbonate groups of PVP ring do not interact with a ligand: they are kept by the previous membranes with the hydrogen bonds.

(c) Water molecules, kept by hydrophobic fragments of PVP chains, are right next to active complex-forming sites. These molecules can have significant effect on the intermolecular interactions of PVP with additional reagent.

(d) As a result of highly polarized group (ions of hydroxonium), chemical hydration of this group by water molecules can occur [57].

Two percent of pyrrolidone rings can participate in the hydration.

As a result of the high sorption ability of PVP due to numerous physical and chemical interactions with water, it is characterized by significant hygroscopicity. It can sorb and keep large amount of water from the air (**Figure 4**). Moreover, curves of sorption and desorption of water from the air do not match [58].

The desorption curve is at a higher level than sorption curve, indicating a high water-binding power by PVP links, which are characterized by previous interactions (**Figure 5**).

Due to the specificity of the interaction of PVP with water, the coefficient of swelling and water sorption for copolymers on its basis is much higher than those inherent to structured monomer matrices. For PVP copolymers, the swelling coefficient is 1.22…1.35, and the water content is within the range of 47–60% (**Table 10**) [53].

At the same time, it was established that the water sorption and the swelling coefficient practically do not depend on the degree of cross-linking of the polymer matrix (by the amount of dimethacrylate). Water sorption can be the same for both the greater and the smaller cross-link density, if the amount of PVP in the (co)polymer is changed [59].
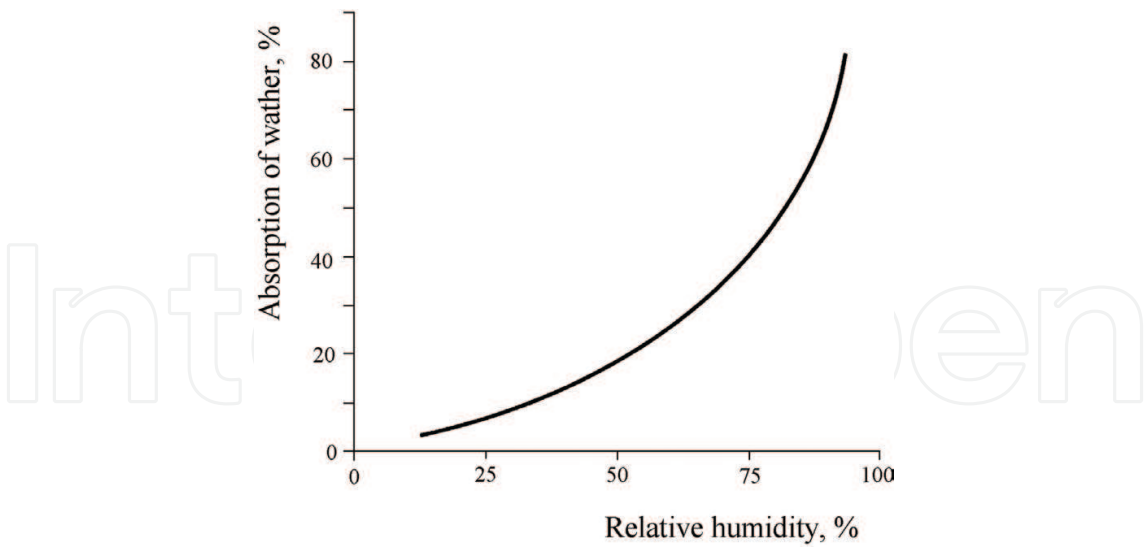
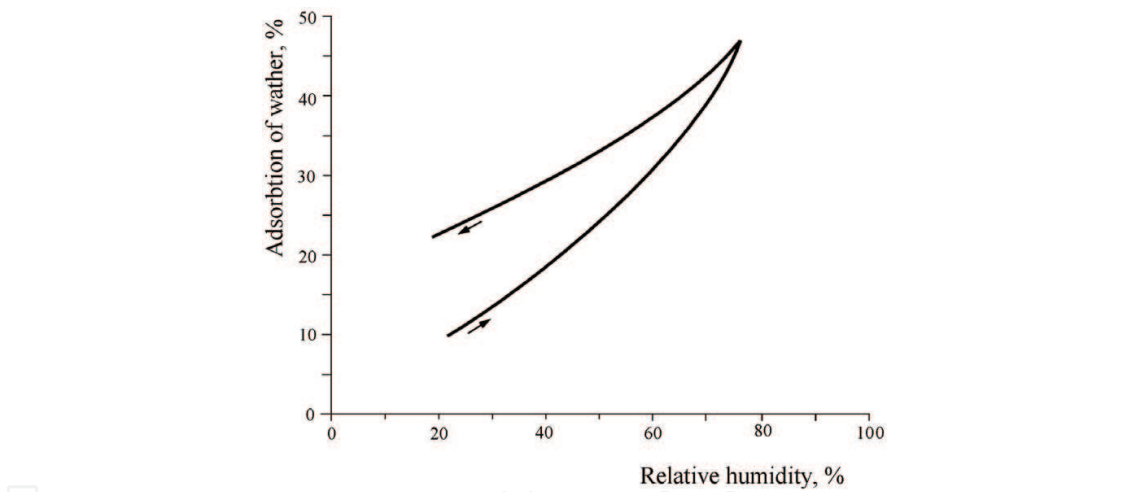**Figure 4.** Adsorption of water by PVP from the atmosphere (25°C) for 7 days.

Figure 5. Adsorption and desorption of water by PVP from atmosphere (25°C) [58].

Material of membranes	Heparin sorption	Heparin desorption for 24 h (%)			$K_{NaCl} \cdot 10^5$
	$(10^{-3}\ u/m^2)$	pH = 2.7	pH = 7	pH = 9.1	$(mole \cdot m^{-2} \cdot h^{-1})$
PHEMA	115	4	8	80	212/242[*]
PVP-gr-PHEMA	550	0	0	2	848/865[*]
Methyl cellulose	126	8	5	95	–

Comments: $\delta = 200\ \mu m$; K_{NaCl} is a permeability coefficient for NaCl; [*]for heparinized membranes.

Table 10. Heparin immobilization by membrane surface and their permeability.

4. Application of the practical use of hydrogels based on copolymers of PVP and (meth)acrylates

4.1. Sorption-active granular copolymers of methacrylic acid esters with polyvinylpyrrolidone [60]

Granular copolymerization of 2-hydroxyethyl methacrylate and glycidyl methacrylate with polyvinylpyrrolidone in inert solvents was studied. In suspension (co)polymerization of HEMA with PVP using both PVP and PVA, as stabilizers and also magnesium hydroxide, we obtained spherical particles of satisfactory polydispersity.

The copolymers synthesized are promising as polymer systems for prolonged and controlled drug release. Spherical polymeric particles of size 0.25…2 mm were prepared by suspension copolymerization of the formulations of 2-hydroxyethyl methacrylate and glycidyl methacrylate with polyvinylpyrrolidone. The size and polydispersity of the particles can be controlled by varying the process parameters. The copolymers synthesized exhibit an increased ability to sorb anionic substances, with their subsequent prolonged release in alkaline medium. The composition and particle size of the (co)polymers determine the fields of their application and their performance in prolonged drug release systems.

We researched the effect of the main component ratio of the initial composition on sorption-desorption properties of the granulated polymers based on the results shown in **Figure 6**.

As seen from the obtained results, the lowest observed sorption capacity have homopolymers based on HEMA (**Figure 6**, curve 1). And, efficient sorption has been observed in the first 4 h of the process and continue virtually unchanged. The granulated drug carriers of "Sferogel" provide an effective control of release at a constant rate during the first 8…1 h (**Figure 7**, curve 2).
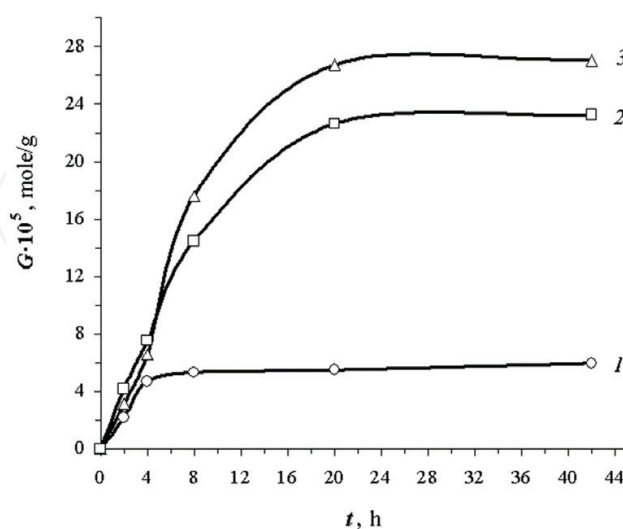

Figure 6. The kinetic curves of diclofenac sodium sorption (G) by granulated hydrogel polymer (SG): HEMA:PVP, wt. p.: (1) 10:0 (SG-1); (2) 8:2 (SG-2); (3) 7:3 (SG-3); $d_{ev.}$ = 640 μm.
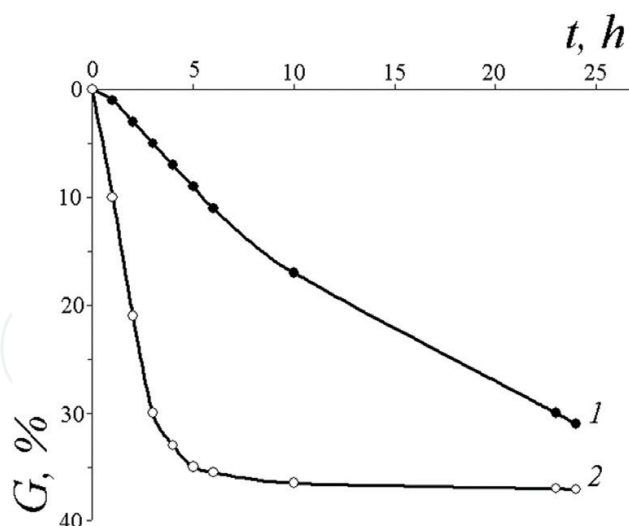
Figure 7. Kinetic curves of diclofenac sodium desorption: (1) for film composite materials filled with SG (HEMA:PVP:SG-2:H$_2$O = 8:2:1:15 wt. p.) and (2) for SG-2.

If the granules are placed in a hydrogel film, the induction period of 1 h is observed during release when the drugs diffuse from the granules through the film; then, the stable and prolonged release takes place into the environment during the day (**Figure 7**, curve 1).

4.2. High-hydrophilic and thromboresistive dialysis membranes [61, 62]

Development of hemodialysis membranes, cardiovascular implants, and other artificial organs put forward the problem of thromboresistive material creation. One of the effective ways of thromboresistance increase is immobilization of heparin, which is a natural blood anticoagulant, over material surface. The main problem of heparin immobilization by polymeric membranes is its permanent minimal desorption at a contact with blood.

Netted of HEMA/PVP copolymers are perspective compounds for the production of dialysis membranes. The presence of PVP ionic groups in the composition of mentioned copolymers assumes the expansion of biochemical and sorption characteristics and obtaining of membranes with additional functions on their basis.

Hydrogel membranes were obtained by graft polymerization of HEMA over PVP (molecular mass was 10…50·10^3) in an aqueous medium, which allowed to combine the synthesis stage and membrane swelling. The saturation of membranes with heparin was realized in glycerol buffer solution (1 M glycerin solution, pH = 2.7), which contained 250,000 units of heparin in 1 l. The amount of sorbed and desorbed heparin was determined by photocolorimetry, based on quantitative determination of heparin and methylene blue complex. Synthesized hydrogel membranes with PVP links have advanced the immobilization ability relative to heparin (**Table 10**).

PVP–heparin complex is so strong, that heparin does not desorb for 24 hours (see Table 10) from the membranes keeping in solutions with different pH (glycin buffer solution with

pH=2.7, physiological solution with pH = 7, and solution of sodium tetraboric acid with pH = 9.1). Here, the selective transport characteristics of membranes are changed insignificantly. As for membranes based on polyHEMA and modified cellulose, there is an insignificant precipitation of anticoagulant in acid and neutral media, while in alkaline medium, it grows to 80…95%.

We have established that the presence of –OH and N–C = O hydrophilic groups in the composition of membrane copolymers increases their sorption ability which is characterized with water content (**Table 11**). The increase of PVP content multiplies dialysis permeability (K_{NaCl}) of hydrogel membranes based on HEMA/PVP, but their strength falls down (**Table 11**). Hence, changing hydrogel chemical structure, it is possible to change permeability of membranes on the basis of HEMA/PVP copolymers.

4.3. Hydrogel membranes based on cross-linked copolymers of polyvinylpyrrolidone [63]

At the same time, the hydrogel membranes based on HEMA/PVP copolymers have higher sorption properties compared with HEMA copolymers and higher penetrability for water and several low molecular mass compounds (**Table 12**).

It is interesting that the mass between cross-links does not directly depend upon the solvent polarity. One would expect such a dependence of the given "loosing" effect on the PVP molecules. However, when the solvent amount exceeds its maximum sorption by the polymeric matrix at swelling equilibrium, the already mentioned phase separation occurs (**Table 12**).

Thus, the control of the initial mixture composition via complex formation is an effective method of structure and penetration control for hydrogel membranes based on hydroxyalkyl methacrylates and polyvinylpyrrolidone. Membranes may be recommended for encapsulation and creation of prolonged forms of drug's controlled release and hemodialysis, as well as for fractionating and concentrating of high molecular mass compounds, including biological media.

Contents of the components (mass parts)		Membrane tensile strength (MPa)	Water content (%)	K_{NaCl} (mole·m^{-2}·h^{-1})
HEMA	PVP			
100	—	0.53	40	127
91	9	0.46	45	293
82	18	0.40	48	412
77	23	0.31	53	506
69	31	0.22	61	611

Comments: δ = 200 μm; K_{NaCl} is a permeability coefficient for NaCl.

Table 11. Properties of hydrogel membranes based on HEMA/PVP.

Contents of the components (mass parts)				Water content (%)	K·10^4 (m^3/m^2·h)	Penetration coefficient[*] (mole/m^2·h)		
HEMA	PVP	H$_2$O	DMSO			NaCl	Carbamide	Saccharose
100	—	100	—	40	5	80	13	5
80	20	100	—	48	52	181	36	14
80	20	95	5	48	55	193	—	—
80	20	90	10	47	57	212	—	—
80	20	80	20	47	63	240	—	—
80	20	200	—	55	74	234	59	30
80	20	300	—	61	90	263	60	31
70	30	100	—	53	71	232	59	30
50	50	100	—	61	102	274	65	33

Comments: [*]for δ = 200 μm; K, coefficient of water permeability; optical transmission coefficient is 90–96% for experiments 1–5, 8, and 9; opaque membranes have been obtained in experiments 6 and 7.

Table 12. Sorption-diffusion properties of hydrogel membranes.

4.4. Polyvinylpyrrolidone cross-linked copolymers for capsulated particles of drugs [64, 65]

Copolymers synthesized in the form of membranes were effective capsulated agents of solid drugs. In dry state, while storing, they act as protective envelope, but while operation they are able to swell in the physical solution and become permeable. The transferring mechanism of components, including drugs, from encapsulated particles involves several stages (**Figure 8**):

- Swelling of the hydrogel membrane

- Molecular diffusion inside the capsule

- Mass transfer through the hydrogel membrane to the surrounding solution

The used capsule is excreted naturally, without causing any collateral damage to the body.

We also examined the drug release by spherical particles because they model the behavior of prolonged drug while operation.

Thus, we established the relationship between synthesis conditions, structure, and sorption-desorption properties of PVP cross-linked copolymers, what offers their application as carriers for the systems of drug's directional and controlled release.

4.5. Soft contact lenses [66]

It should be noted that the change of the structure and composition of copolymers may considerably influence the size of refraction index n_D. This was consequently used for optimization of
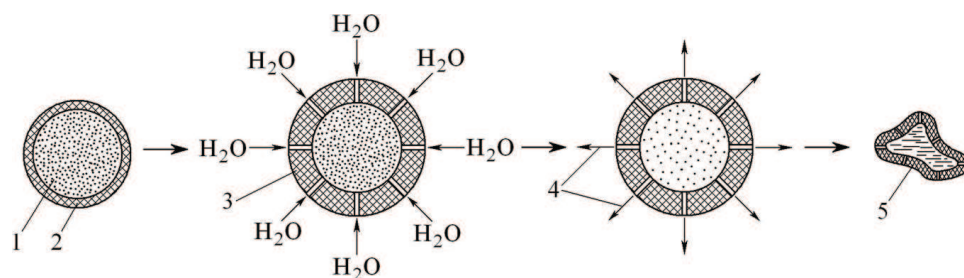
Figure 8. The scheme of component transfer from encapsulated particles: (1) dosage form, (2) hard polymeric shell, (3) swollen hydrogel, (4) release of dosage form, and (5) used capsule.

copolymer composition for contact lenses. It allowed to manufacture correctional soft contact lenses "Akrylan-LPI" with the following operational properties (**Table 13**).

Good permeability for a series of substances, including medicinal solutions, compatibility with alive tissues, and acceptability, has caused the use of the synthesized copolymers for medical ophthalmologic elements of the various geometric shapes. Significant advantage of contact lenses based on PVP copolymer is an essential retention of UV rays and increased oxygen permeability. It provides the lens comfort while long staying on the eye's cornea.

The comparative clinical tests of a condition of an acuteness of vision of an eye without correction and portable spectacle correction were carried out in Lviv Railway Clinical Hospital. From 163 patients without having correction of an acuteness of vision less 0.1 after corrections by contact lenses, an acuteness of vision has increased more than in 80% and has made 0.85–1.0. Researches of a condition of an epithelial integument of a cornea carried out in a various lines after acclimatization at all patients have shown that infringement of integrity of a cornea epithelium does not occur. And, only at six patients after long continuous application of lenses (more than 3 days), mild inflammation of an epithelium was observed.

In this, application of soft hydrophilic contact lenses in treatment of eye diseases is a new promising approach. It substitutes surgical methods in treatment of burns, prevents a symblepharon formation, allows a late keratoplastic, improves results, and decreases treatment duration with high social and economic impact.

Properties in hydrated condition	Parameter meaning
Absorption of water (%)	51
Oxygen permeability ($\times 10^{10}$ m$^2 \cdot$s^{-1})	1.2
Water permeability ($\times 10^4$ m$^3 \cdot$m$^{-2} \cdot$h^{-1})	52
NaCl permeability (mole$\cdot$m$^{-2} \cdot$s^{-1})	180
Toughness at a stretching (MPa)	0.4
Relative tensile elongation (%)	250
Permeability of light (%)	96
Refraction index (n_D)	1.4253

Table 13. The characteristics of a polymeric material for soft contact lenses "Akrylan-LPI".

Clinical trial batch of 460 soft contact lens materials of "Akrylan-LPI" in the Laboratory of contact correction of the Filatov Institute of Eye Diseases and Tissue Therapy (Odesa) has been conducted. The comparative study on eye visual acuity, corrected with soft contact lens material "Akrylan-LPI" lenses and contact lens from polyHEMA, has been held on 180 eyes in order to evaluate the optical correction of soft contact lenses.

5. Conclusions

The charge-transfer complex between polyvinylpyrrolidone and 2-hydroxyethyl methacrylate has been determined to affect the polymerizability of PVP/HEMA formulations and the structure of the resulting copolymers. Increasing Kst for the PVP/HEMA complexes has been shown to increase the cross-linking degree of the formed polymer network. It has been revealed that loosely cross-linked PVP/HEMA copolymers and hydrogels based on them can be developed without any radical initiator or in the presence of iron(II) and iron(III) ions. The synthesized hydrogels have increased water content, and their mechanical properties can be easily tuned in a wide range. Moreover, the hydrogels possess high permeability for low-molecular water-soluble substances. Hydrogels also are able for selective sorption of drugs, including a blood anticoagulant heparin. The developed hydrogel materials have been widely tested in industry and recommended for manufacturing various products of medical applications.

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